

AMENDMENTS TO THE CLAIMS

Claim 1 (currently amended): A method of reducing nephrotoxicity in an individual during radioimmunotherapeutic treatment of a pathophysiological condition, comprising:

administering a pharmacologically effective dose of ~~at least one adjuvant, wherein said adjuvant is a chelator, a diuretic, a competitive metal blocker, or a combination thereof, effective for preventing accumulation of alpha-particle emitting daughters of actinium-225 radioisotope in kidneys,~~ a competitive metal blocker consisting of bismuth subnitrate or bismuth subcitrate alone or said competitive metal blocker in combination with one or both of a chelator(s) or a diuretic(s);

administering an actinium-225 radioimmunoconjugate to treat the pathophysiological condition; and

preventing accumulation of said alpha particle-emitting daughters of said actinium-225 within the kidneys of the individual via interaction between one or more of said competitive metal blocker or said chelator or said diuretic ~~adjuvant~~ and said ²²⁵Ac daughters or the kidney tissue or a combination thereof thereby reducing nephrotoxicity during the radioimmunotherapeutic treatment.

Claim 2 (currently amended): The method of claim 1, wherein one or more of said adjuvant(s) competitive metal blocker, said chelator or said diuretic is administered prior to administering said actinium-225

radioimmunoconjugate, one or more of said ~~adjuvant(s)~~ competitive metal blocker, said chelator or said diuretic continuing to be administered after said actinium-225 radioimmunoconjugate.

Claim 3 (canceled).

Claim 4 (currently amended): The method of claim 1, wherein said chelator is a dithiol chelating agent, 2,3 dimercapto-1-propane sulfonic acid, meso 2,3-dimercapto succinic acid, [[or a]] diethylenetriamine pentaacetic acid, calcium diethylenetriamine pentaacetic acid, or zinc diethylenetriamine pentaacetic acid

Claim 5 (currently amended): The method of claim 1, wherein said diuretic is furosemide, chlorthiazide, hydrochlorothiazide[[,]] or bumex ~~or other~~ ~~loop-diuretic~~.

Claim 6 (canceled).

Claim 7 (original): The method of claim 1, wherein said ²²⁵Ac daughter is bismuth-213, francium-221 or a combination thereof.

Claim 8 (original): The method of claim 1, wherein said actinium-225 radioimmunoconjugate comprises an actinium-225 bifunctional chelant and a monoclonal antibody.

Claim 9 (original): The method of claim 8, wherein said actinium-225 radioimmunoconjugate is [²²⁵Ac] DOTA-HuM195.

Claim 10 (original): The method of claim 1, wherein said pathophysiological condition is a cancer or an autoimmune disorder.

Claim 11 (original): The method of claim 1, wherein said cancer is a solid cancer, a disseminated cancer or a micrometastatic cancer.

Claim 12 (original): The method of claim 11, wherein said cancer is myeloid leukemia.

Claim 13 (currently amended): A method of reducing nephrotoxicity in an individual during radioimmunotherapeutic treatment a pathophysiological condition, comprising:

administering a pharmacologically effective dose of a diuretic in combination with a chelator;

administering an actinium-225 radioimmunoconjugate to treat the cancer; and

preventing accumulation of bismuth-213 daughters and francium-211 daughters of said actinium-225 within the kidneys of the individual by scavenging thereof with said diuretic and said chelator thereby reducing nephrotoxicity during the radioimmunotherapeutic treatment.

Claim 14 (currently amended): The method of claim 13, wherein one or both of said diuretic or said chelator is administered prior to administering said ^{225}Ac radioimmunoconjugate, one or both of said diuretic or said chelator continuing to be administered after said ^{225}Ac radioimmunoconjugate.

Claim 15 (currently amended): The method of claim 13, wherein said chelator is a dithiol chelating agent, 2,3 dimercapto-1-propane sulfonic acid, meso 2, 3-dimercapto succinic acid, diethylenetriamine pentaacetic acid, calcium diethylenetriamine pentaacetic acid or zinc diethylenetriamine pentaacetic acid.

Claims 16-17 (canceled).

Claim 18 (currently amended): The method of claim 13 ~~[[16]]~~, wherein said diuretic is furosemide, chlorthiazide, hydrochlorothiazide~~[[,]]~~ or bumex ~~or other loop diuretic.~~

Claim 19 (original): The method of claim 13, wherein said ^{225}Ac radioimmunoconjugate comprises an actinium-225 bifunctional chelant and a monoclonal antibody.

Claim 20 (original): The method of claim 19, wherein said ^{225}Ac radioimmunoconjugate is [^{225}Ac] DOTA-HuM195.

Claim 21 (original): The method of claim 13, wherein said pathophysiological condition is a cancer or an autoimmune disorder.

Claim 22 (original): The method of claim 21, wherein said cancer is a solid cancer, a disseminated cancer or a micrometastatic cancer.

Claim 23 (original): The method of claim 22, wherein said cancer is myeloid leukemia.

Claim 24 (original): A method of reducing nephrotoxicity in an individual during radioimmunotherapeutic treatment of a pathophysiological condition, comprising:

administering a pharmacologically effective dose of a diuretic;

administering an actinium-225 radioimmunoconjugate to treat the cancer; and

preventing accumulation of francium-211 daughters of said actinium-225 within the kidneys of the individual by inhibiting reabsorption of francium-211 therein with said diuretic thereby reducing nephrotoxicity during the radioimmunotherapeutic treatment.

Claim 25 (original): The method of claim 24, wherein said diuretic is administered prior to administering said ^{225}Ac radioimmunoconjugate, said diuretic continuing to be administered after said ^{225}Ac radioimmunoconjugate.

Claim 26 (currently amended): The method of claim 24, wherein said diuretic is furosemide, chlorthiazide, hydrochlorothiazide[[,]] or bumex ~~or other loop diuretic~~.

Claim 27 (original): The method of claim 24, wherein said ^{225}Ac radioimmunoconjugate comprises an actinium-225 bifunctional chelant and a monoclonal antibody.

Claim 28 (original): The method of claim 27, wherein said ^{225}Ac radioimmunoconjugate is [^{225}Ac] DOTA-HuM195.

Claim 29 (original): The method of claim 24, wherein said pathophysiological condition is a cancer or an autoimmune disorder.

Claim 30 (original): The method of claim 29, wherein said cancer is a solid cancer, a disseminated cancer or a micrometastatic cancer.

Claim 31 (original): The method of claim 30, wherein said cancer is myeloid leukemia.

Claim 32 (currently amended): A method of improving radioimmunotherapeutic treatment of cancer in an individual, comprising:

administering a pharmacologically effective dose of a diuretic and a chelator;

administering an actinium-225 radioimmunoconjugate; and

scavenging bismuth-213 daughters of the actinium-225 and inhibiting renal uptake of francium-211 daughters of the actinium-225 with said diuretic and said chelator to reduce nephrotoxicity in the individual during the treatment, thereby increasing the therapeutic index of the actinium-225 to improve the treatment for said cancer.

Claim 33 (currently amended): The method of claim 32, wherein one or both of said diuretic or said chelator is administered prior to administering said ²²⁵Ac radioimmunoconjugate, one or both of said diuretic or said chelator continuing to be administered after said ²²⁵Ac radioimmunoconjugate.

Claims 34 (currently amended): The method of claim 32, wherein said chelator is a dithiol chelating agent, 2,3 dimercapto-1-propane sulfonic acid, meso 2,3-dimercapto succinic acid, diethylenetriamine pentaacetic acid, calcium diethylenetriamine pentaacetic acid, or zinc diethylenetriamine pentaacetic acid.

Claims 35-36 (canceled).

Claim 37 (currently amended): The method of claim 32 ~~[[35]]~~, wherein said diuretic is furosemide, chlorthiazide, hydrochlorothiazide~~[[,]]~~ or bumex or other loop diuretic.

Claim 38 (currently amended): The method of claim ~~[[35]]~~ 32, wherein said ²²⁵Ac radioimmunoconjugate comprises an actinium-225 bifunctional chelant and a monoclonal antibody.

Claim 39 (original): The method of claim 38, wherein said ²²⁵Ac radioimmunoconjugate is [²²⁵Ac] DOTA-HuM195.

Claim 40 (currently amended): The method of claim ~~[[35]]~~ 32, wherein said cancer is a solid cancer, a disseminated cancer or a micrometastatic cancer.

Claim 41 (original): The method of claim 40, wherein said cancer is myeloid leukemia.

Claim 42 (original): A method of improving radioimmunotherapeutic treatment of cancer in an individual, comprising:

administering a pharmacologically effective dose of a diuretic;

administering an actinium-225 radioimmunoconjugate; and

inhibiting renal uptake of francium-211 daughters of the actinium-225 with said diuretic to reduce nephrotoxicity in the individual during the treatment thereby increasing the therapeutic index of the actinium-225 to improve the treatment for said cancer.

Claim 43 (original): The method of claim 42, wherein said diuretic is administered prior to administering said ^{225}Ac radioimmunoconjugate, said diuretic continuing to be administered after said ^{225}Ac radioimmunoconjugate.

Claim 44 (currently amended): The method of claim 42, wherein said diuretic is furosemide, chlorthiazide, hydrochlorothiazide[[,]] or bumex ~~or other loop diuretic~~.

Claim 45 (original): The method of claim 42, wherein said ^{225}Ac radioimmunoconjugate comprises an actinium-225 bifunctional chelant and a monoclonal antibody.

Claim 46 (original): The method of claim 45, wherein said ^{225}Ac radioimmunoconjugate is [^{225}Ac] DOTA-HuM195.

Claim 47 (original): The method of claim 42, wherein said cancer is a solid cancer, a disseminated cancer or a micrometastatic cancer.

Claim 48 (original): The method of claim 47, wherein said cancer is myeloid leukemia.

Claim 49 (currently amended): A method of increasing the therapeutic index of an actinium-225 radioimmunoconjugate during treatment of a pathophysiological condition in an individual comprising:

inhibiting renal uptake of at least one alpha particle-emitting daughter of actinium-225 comprising: administering a pharmacologically effective amount of ~~an adjuvant, wherein said adjuvant is a chelator, one or both of a~~ diuretic ~~[[,]]~~ or a competitive metal blocker consisting of bismuth subnitrate or bismuth subcitrate or one or both of said diuretic or said competitive metal blocker in combination with a chelator, or a combination thereof effective for preventing accumulation of alpha particle emitting daughters of Actinium-225 whereby nephrotoxicity is reduced during the treatment due to prevention of accumulation of daughters of said actinium-225, thereby increasing the therapeutic index of said actinium-225 radioimmunoconjugate.

Claim 50 (canceled).

Claim 51 (previously presented): The method of claim 49, wherein said chelator and/or said diuretic and/or said competitive metal blocker are administered prior to treatment with said actinium-225 radioimmunoconjugate, said chelator and/or said diuretic continuing to be administered after said actinium-225 radioimmunoconjugate is administered to the individual.

Claim 52 (currently amended): The method of claim 49, wherein said chelator is a dithiol chelating agent, 2,3 dimercapto-1-propane sulfonic acid, meso 2,3-dimercapto succinic acid, diethylenetriamine pentaacetic acid, calcium diethylenetriamine pentaacetic acid, or zinc diethylenetriamine pentaacetic acid

Claim 53 (currently amended); The method of claim 49, wherein said diuretic is furosemide, chlorthiazide, hydrochlorothiazide[[.]] or bumex ~~or other loop diuretic~~.

Claim 54 (canceled).

Claim 55 (previously presented): The method of claim 49, wherein said chelator scavenges the ²²⁵Ac daughter bismuth-213.

Claim 56 (previously presented): The method of claim 49, wherein said diuretic inhibits reabsorption of the ^{225}Ac daughter francium-211.

Claim 57 (currently amended): The method of claim 49, wherein said competitive metal ~~binder~~ blocker prevents binding of the ^{225}Ac daughter bismuth-213.

Claim 58 (original): The method of claim 49, wherein said actinium-225 radioimmunoconjugate is [^{225}Ac] DOTA-HuM195.

Claim 59 (original): The method of claim 49, wherein said pathophysiological condition is a cancer or an autoimmune disorder.

Claim 60 (original): The method of claim 59, wherein said cancer is a solid cancer, a disseminated cancer or a micrometastatic cancer.

Claim 61 (original): The method of claim 60, wherein said cancer is myeloid leukemia.